UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,634	11/16/2005	Xiangping Qian	09367.0012-00000	1369

22852 7590 07/16/2008

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
07/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,634	QIAN ET AL.	
	Examiner	Art Unit	
	SUN JAE Y. LOEWE	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-11,13 and 17* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11, 13 and 17 are pending in the instant application.

Response to Amendment

2. Applicant's amendments to the claims filed on April 8, 2008 have been fully considered. The following grounds of rejection are overcome and thus hereby withdrawn: a) 35 USC 102; b) 35 USC 103.

3. The following ground of rejection is maintained and hereby made FINAL: 35 USC 112 2nd paragraph. See response to amendment below, Section 9.

4. The following new ground of rejection was necessitated by amendment: 35 USC 112 1st paragraph. See below, Sections 7 and 8.

Election/Restrictions

5. Notwithstanding the 35 USC 112 2nd paragraph rejection of the generic claims, the search and examination was extended to the full scope of claim 1. All compounds of Formula I were rejoined and fully examined for patentability.

The compounds appear to be novel and unobvious over the prior art (see Section 10). However, the generic claims do not comply with 35 USC 112 1st paragraph. Therefore, a new ground of rejection, necessitated by the rejoinder of non-elected species, is set forth herein (Sections 7 and 8).

Claim Objections

6. Claim 4 objected to for depending on a base rejected claim but would be allowable if re-written in independent form.

New Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 5-11, 13 and 17 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

I. ***Scope of Claims***

Compounds of Formula I.

The following variables are claimed broader than what is supported by the disclosure: R4, R5, R6.

II. ***Scope of Disclosure***

Reduction to Practice/Chemical/Structural Formula:

The compounds reduced to practice support

R4:	H, alkyl, phenyl, pyridinyl
R5:	alkyl
R6	phenyl.

Correlation between Structure and Function:

A correlation between structure and function, for the instantly claimed genus of compounds, is neither known in the art nor disclosed in the specification. Thus, it is not known what unrepresented species will have the instant activity.

III. *Analysis of Fulfillment of Written Description Requirement:*

The structure/activity relationship (SAR) for binding and activity is elucidated upon analysis of IC_{50}/EC_{50} data of multiple compounds with various types of structural modifications. These types of studies provide insight into the structural limitations that are required for activity, ie. specific structural elements tolerated for the claimed activity. In the absence of such correlation, it is not possible to determine what structural modifications will allow for the preservation of the desired activity.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1-3, 5-11, 13 and 17; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds

claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(Enablement)

8. Claims 11-3, 5-11, 13 and 17 rejected under 35 U.S.C. 112, first paragraph. The specification is *enabling* for the use of the compounds that have adequate written description (see Section 8). The specification is *not enabling* for the use of compounds not supported by the disclosure.

In conclusion, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

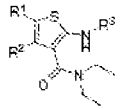
The breadth of the claims
Compounds not supported by the disclosure (see above section 7.I and 7.II.).

The nature of the invention
The compounds are disclosed to be KSP inhibitors. An alternate utility is neither disclosed in the specification nor known in the art for this genus of compounds.

The state of the prior art/level of ordinary skill/level of predictability
The level of ordinary skill is high, but the level of predictability in the art is low. Although SAR studies are not available for the instantly claimed genus of compounds, these studies have been disclosed for other compounds with the same utility, see example below.

- Pinkerton et al., Tables 2 and 3:

Table 6. Optimization of core and pendant groups



Compound	R^1	R^2	R^3	ATPase IC_{50}[a] (μM)	MPM-2 Cytoblot EC_{50}[a] (μM)	Cytotoxicity 60 h EC_{50}[a] (μM)
12	-H	-H		>100	NA[b]	NA[b]
13	$-CH_3$	$-CH_3$		25(5)	29(11)	>30
14	$-(CH_2)_5-$			9.9(2.1)	2.2(0.2)	3.1(1.9)
15	$-(CH_2)_4-$			1.3(0.4)	0.48(0.13)	2.0(0.2)
16	$-(CH_2)_3-$			4.3(0.9)	5.0(0.8)	13(5)
17	$-(CH_2)_4-$			13(2)	4.3(0.8)	29.4(0.1)
18	$-(CH_2)_4-$			36(19)	>30	NA[b]
19	$-(CH_2)_4-$			17(8)	>30	>30
20	$-(CH_2)_4-$			23(5)	20(7)	>30
21	$-(CH_2)_4-$			33(9)	34(18)	>30
22	$-(CH_2)_4-$			20(8)	>30	>30

[a] Value represents the mean of three experiments with standard deviations shown in parentheses.
[b] NA, not active < 30 μM.

As discussed in section 7, it is not known what structural limitations are required for preservation of activity within the genus. In view of the low level of predictability one of ordinary skill would not know what structural modifications within the unrepresented genus (ie. unrepresented by the disclosure), if any, would lead to compounds that are active.

The amount of direction provided by the inventor/existence of working examples
Direction and working examples are limited to the genus of compounds that have adequate written description support (see Section 7.II).

The quantity of experimentation needed to make or use the invention

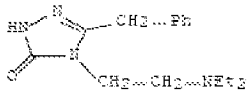
It is not known which of the unrepresented compounds meet the structural requirements for activity. Thus, one of ordinary skill would not be enabled by the disclosure to make/use the claimed KSP inhibitors. The amount of experimentation needed to practice the invention is undue. Further, absent an alternate utility, one of ordinary skill would not be enabled to use the compounds within the genus that are not adequately supported in the disclosure.

Maintained Claim Rejections – 35 USC § 112 2nd Paragraph

9. The 35 USC 112 2nd paragraph rejection of claim 1 is maintained. The claim may still be interpreted as a mixture of pharmaceutically acceptable salts. To overcome this ground of rejection the following correction is suggested: replace "or pharmaceutically acceptable salts or mixtures thereof." with "or a pharmaceutically acceptable salt or mixture thereof".

Allowable Subject Matter

10. The compounds of Formula I appear to be novel and non-obvious over the prior art. The closest reference is, for example, the compound disclosed by Pesson et al.



which neither anticipates nor makes obvious the instant invention.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe, Ph.D./
7-3-2008

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626